PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 32741P WO	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2005/004047	International filing date *(day/month/year)* 15.04.2005	Priority date *(day/month/year)* 16.04.2004
International Patent Classification (IPC) or national classification and IPC INV. A61K38/05 A61P25/06 A61K31/16 A61K31/165		
Applicant SCHWARZ PHARMA AG		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
16.02.2006	13.09.2006
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Langer, Oliver Telephone No. +31 70 340-1972

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2005/004047

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-36	as originally filed
Claims, Numbers	
1-38	as originally filed
Drawings, Sheets	
1/1	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	33,34,37,38
	No:	Claims	1-32,35,36
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-38
Industrial applicability (IA)	Yes:	Claims	1-38
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1. Reference is made to the following document:

D1: WO 02/15922 A (RESEARCH CORPORATION TECHNOLOGIES, INC) 28. February 2002 (2002-02-28)

V.2. Novelty (Article 33(2) PCT)

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-32, 35 and 36 is not new in the sense of Article 33(2) PCT.

The document D1 (WO-A-02/15922)

...discloses the use of compounds according to formula (Ib) for the treatment of migraine headaches (abstract).

The explicitly mentioned compounds of claims 14 and 24 of the application are also specifically claimed in document D1 (claims 15 and 34). Concerning the selection of enantiomers, the "D stereoisomer is preferred" in document D1 (page 31, line 6). See also the other passages cited in the search report.

The knowledge of CSD involvement in the development of migraine is not limiting the claims which are clearly directed to the treatment of migraine, see, e.g., page 1, paragraph 1; page 4, last paragraph to page 5, fist paragraph; page 8, lines 30 and 31; page 11, last paragraph. This applies regardless of the mechanism involved in migraine development.

The document D1 is clearly relating to the treatment of migraine and therefore relevant for novelty.

The disclosure of document D1 is novelty-destroying for the subject-matter of claims 1-32, 35 and 36.

V.3. Inventive Step (Article 33(3) PCT)

V.3.1. Claims 33, 34, 37 and 38

V.3.1.1. The claims 33 and 34 relate to the use of the compounds of the application in combination with "a further active agent for the prevention, alleviation or/and treatment of headache or/and CSD-associated disorders" (claim 33).

V.3.1.2. The claims 37 and 38 relate to pharmaceutical compositions comprising a compound of the application in combination with "a further active agent for the prevention, alleviation or/and treatment of headache or/and CSD-associated disorders" (claim 37).

V.3.1.3. Analysis of inventive step for the combination of pharmaceutically active compounds:
The act of combining two active compounds A and B for use in the treatment of a disease X is not considered to involve an inventive step if both A and B are already separately known to be effective in the treatment of X, unless an unexpected effect is obtained by combining A and B.

Knowing about the properties of A and B, the skilled person would expect at least some effect in the treatment of X when A and B are combined, unless indications to the contrary are available from the prior art.

Likewise, for a claim to the combination of A and B as a pharmaceutical combination, if A and B are already separately known for their use in therapy, the combination is not inventive.

Therefore, any claims to combinations of compounds for which no unexpected effect has been demonstrated in the application cannot be considered to involve an inventive step.

V.3.1.4. The claimed pharmaceutical activity of the compounds of the application (A) are known from D1. The second component (B) is defined by its applicability in the claimed therapeutic application (X).

V.3.1.5. The subject-matter of present claims 33, 34, 37 and 38 consequently lacks the

presence of an inventive step in the sense of Article 33(3) PCT in view of the disclosure of document D1.

V.3.2. Claims 1-32, 35 and 36

The claims 1-32, 35 and 36 are not novel in view of the disclosure of document D1, see section V.2.

These claims consequently also lack an inventive step since they are obvious in view of the document D1 as closest prior art.

V.3.3. The subject-matter of present claims 1-38 lacks an inventive step in the sense of Article 33(3) PCT.

V.4. Industrial applicability (Article 33(4) PCT)

Present claims 1-38 relate to the provision of pharmaceutical compositions and to the second or further medical use of peptidic compounds and meet the requirements of Article 33(4) PCT.